Applicant : Eleftheria Maratos-Flie

Serial No.: 09/159,068

Filed: September 23, 1998

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In the abstract:

At page 47, please delete the abstract of the invention and insert the following new abstract.

Methods for promoting or inhibiting appetite are provided. The methods include administering to the subject an effective amount of melanocyte concentrating hormone (MCH) or an agonist or antagonist thereof.

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In the Claims:

Please amend the claims as follows.

- 8. (Amended) A method of inhibiting [eating] appetite, or the gain of weight, in a subject comprising: identifying a subject in need of inhibiting appetite or weight gain; and administering an effective amount of an antagonist of melanocyte concentrating hormone (MCH) [MCH] to said subject, wherein the antagonist is a peptide analog of MCH.
- 9. (Reiterated) The method of claim 8, wherein said subject is overweight or exhibits compulsive eating behavior.
- 10. (Reiterated) The method of claim 8, further comprising diagnosing said subject as being at risk for any of compulsive eating behavior, obesity, or eating disorder.
 - 11. (Reiterated) The method of claim 8, wherein said subject is human.
- 12. (Reiterated) The method of claim 8, wherein said subject is administered a second dose of an antagonist of MCH.

Please add new claims 13-24 as follows.

P126 +3. (New residues of MCF

13. (New) The method of claim 8, wherein the peptide analog has one to ten amino acid residues of MCH which have been substituted or deleted.

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3| 44: (New) The method of claim 8, wherein the peptide analog has one to six amino acid residues of MCH which have been substituted or deleted.

32 45. (New) The method of claim 8, wherein the peptide analog has a disulfide ring which includes ten amino acids.

(New) The method of claim 8, wherein the antagonist is at least 50% homologous to MCH.

(New) The method of claim 8, wherein the peptide analog is MCH which has been modified by one or more of the following: shortening the amino terminal region, shortening the carboxy terminal region, contracting the cysteine bridged ring, forming an acyclic analogue, or modifying or substituting an amino acid.

18. (New) The method of claim 8, wherein the antagonist comprises the sequence $R^1-R^2-R^3-R^4-R^5-R^6-R^7-R^8-R^9-R^{10}-R^{11}-R^{12}-R^{13}-R^{14}-R^{15}-R^{16}-R^{17}-R^{18}-R^{19}$ or a fragment thereof, wherein:

R1 is Asp, a conserved amino acid, any D-amino acid, or deleted;

R2 is Phe, a conserved amino acid, any D-amino acid, or deleted;

R3 is Asp, a conserved amino acid, any D-amino acid, or deleted;

R4 is Met or a conserved amino acid, Thr or a conserved amino acid, any D amino acid, or deleted;

R5 is Leu or a conserved amino acid, Met or a conserved amino acid subst, any D amino acid, or deleted;

R6 is Arg, a conserved amino acid, any D-amino acid, deleted, or Cys;

R7 is Cys, or any amino acid;

R8 is Met, a conserved amino acid, or Cys;

R9 is Leu or a conserved amino acid, or Val or a conserved amino acid;

R10 is Gly, or a conserved amino acid;

R11 is Arg, or a conserved amino acid;

R12 is any amino acid other than Val, or other than a conserved amino acid replacement;

R13 is any amino acid other than Tyr, or other than a conserved amino acid replacement;

Cont.

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R14 is any amino acid other than Arg, or other than a conserved amino acid replacement;

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R15 is any amino acid other than Pro, other than a conserved amino acid replacement, or Cys;

R¹⁶ is Cys, or any other amino acid;

R¹⁷ is Trp or a conserved amino acid, an analog of Trp, an amino acid having an aromatic side group, any amino acid other than Trp, other than a conserved amino acid replacement, an amino acid lacking an aromatic side group, deleted, or Cys;

R¹⁸ is Gln or a conserved amino acid, Glu or a conserved amino acid, Trp or a conserved amino acid, an analog of Trp, an amino acid having an aromatic side group, any amino acid other than Trp, other than a conserved amino acid replacement, an amino acid lacking an aromatic side group, or deleted;

R¹⁹ is Val, a conserved amino acid, or deleted;

provided that: if R^6 is Cys, then R^{15} is Cys, the disulfide bridge is formed between the two, and R^7 , R^8 , R^{16} and R^{17} are not Cys; if R^7 is Cys, then R^{16} is Cys, the disulfide bridge is formed between the two, and R^6 , R^8 , R^{15} and R^{17} are not Cys; if R^8 is Cys, then R^{17} is Cys, the disulfide bridge is formed between the two, R^6 , R^7 , R^{15} and R^{16} are not Cys, and R^{18} is Trp or a conserved amino acid, an analog of Trp, an amino acid having an aromatic side group, any amino acid other than Trp, other than a conserved amino acid replacement, an amino acid lacking an aromatic side group, or deleted.

New) The method of claim 18, wherein the peptide analog has a disulfide ring between residues R^7 and R^{16} .

20. (New) The method of claim R^{18} , wherein the peptide analog is deleted for one or both of the residues between R^{18} and R^{19} .

(New) The method of claim 18, wherein the antagonist comprises a sequence corresponding in length to a fragment of MCH selected from the group of MCH(1-16), MCH(2-16), MCH(3-16), MCH(4-16), MCH(5-6), MCH(6-16), or MCH(7-16).

31 22. (New) The method of claim 18, wherein the antagonist is DHCH-Arg^{6,11,14}MCH, or NO₂-Tyr¹³MCH.

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10 23. (New) The method of claim 18, wherein R¹² is an amino acid other than Val.

(New) The method of claim 18, wherein R¹³ is an amino acid other than Tyr.

(New) The method of claim 18, wherein R¹⁴ is an amino acid other than Arg.

(New) The method of claim 18, wherein R¹⁵ is an amino acid other than Pro.

(New) The method of claim 18, wherein R¹⁷ is an amino acid other than Trp.

(New) A method of inhibiting appetite, or the gain of weight, in a subject comprising: identifying a subject in need of inhibiting appetite or weight gain; and administering an effective amount of an antagonist of melanocyte concentrating hormone (MCH) to said subject, wherein the antagonist is a peptide analog of MCH comprising the sequence R¹-R²-R³-R⁴-R⁵-R⁶-R⁷-R⁸-R⁹-R¹⁰-R¹¹-R¹²-R¹³-R¹⁴-R¹⁵-R¹⁵-R¹⁶-R¹⁷-R¹⁸-R¹⁹ or a fragment thereof, wherein:

R1 is Asp, a conserved amino acid, any D-amino acid, or deleted;

R2 is Phe, a conserved amino acid, any D-amino acid, or deleted;

R3 is Asp, a conserved amino acid, any D-amino acid, or deleted;

R4 is Met or a conserved amino acid, Thr or a conserved amino acid, any D amino acid, or deleted;

R5 is Leu or a conserved amino acid, Met or a conserved amino acid subst, any D amino acid, or deleted;

R6 is Arg, a conserved amino acid any D-amino acid, deleted, or Cys;

R7 is Cys, or any aming acid;

R8 is Met, a conserved amino acid, or Cys;

R9 is Leu or a conserved amino acid, or Val or a conserved amino acid;

R10 is Gly, or a conserved amino acid;

R11 is Arg, or a conserved amino acid;

R12 is any amino acid other than Val, or other than a conserved amino acid

replacement;

R13 is any amino acid other than Tyr, or other than a conserved amino acid

replacement;

replacement;

R14 is any amino acid other than Arg, or other than a conserved amino acid